

Ablation Rate of PMMA and Human Cornea With a Frequency-Quintupled Nd:YAG Laser (213 nm)

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Background and Objective: As an alternative to the standard excimer laser used for PRK, we investigated the ablation rate at 213 nm of PMMA, and human corneas under controlled hydration.

Study Design/Materials and Methods: The output of a frequency-quintupled Nd:YAG laser (213 nm) was transformed into a quasi-Gaussian beam. PMMA and corneal lenticles maintained under controlled hydration were ablated until perforation was detected.

Results: The ablation rate of PMMA and cornea at 213 nm were similar to that at 193 nm when radiant exposure was below 200 mJ/cm² and increased gradually between one and two times faster than that at 193 nm when radiant exposure was > 200 mJ/cm².

Conclusions: PMMA and cornea ablation at 213 nm are similar to that at 193 nm and are different from that at 248 nm. The difference between PMMA and cornea ablation rates should be considered when using PMMA to test ablated diopter and smoothness for photorefractive surgery. *Lasers Surg. Med.* 21:179–185, 1997. © 1997 Wiley-Liss, Inc.

Key words: laser corneal surgery; laser-tissue interaction; photorefractive keratectomy; PRK, poly-methyl-methacrylate; solid-state laser; ultraviolet

INTRODUCTION

The ArF excimer laser (193 nm) photo-ablation procedures (photo-refractive keratectomy (PRK) and photo-therapeutic keratectomy (PTK)) can re-profile corneas with high precision and minimal thermal damage zones (< 1 µm) [1–4]. The photoablative effect of other lasers such as KrF (248 nm) [3,5,6], XeCl (308 nm) [3,5], Er:YAG (2.94 µm), Er:YSGG (2.79 µm), CTE:YAG (2.69 µm) [7–9], free electron laser [10], frequency quadrupled (266 nm) [11], and quintupled Nd:

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YAG (213 nm) [12,13], etc., also have been studied. Among these lasers, the frequency-quintupled Nd:YAG laser (213 nm) is promising, because its wavelength and pulse duration are very close to those of the ArF excimer laser. Histologic studies show that the damage zone created by this laser is $< 1 \mu\text{m}$ [12], which is similar to the results obtained with the ArF laser. In addition, the frequency-quintupled Nd:YAG laser is less expensive and more compact than the ArF laser and does not require the use of toxic gases.

Initial *in vitro* and *in vivo* animal studies have demonstrated that the frequency-quintupled Nd:YAG laser (213 nm) coupled to an optical scanning delivery system is capable of reshaping the corneal surface and producing smooth surfaces and transitions [14,15]. Photo-refractive keratectomy (PRK) with the 213 nm laser showed a similar course, including rate of reepithelialization and presence of residual subepithelial haze, and similar histopathologic findings compared to the results with the 193 nm excimer laser PRK in rabbit studies [15]. The purpose of this study was to determine the ablation rate of poly methyl methacrylate (PMMA) and human cornea in a controlled hydration environment with this laser.

MATERIALS AND METHODS

Laser System

A frequency-quintupled Nd:YAG laser (LaserHarmonic, LaserSight, Orlando, FL) (213 nm wavelength, 15 ns pulse duration, 10 Hz repetition rate) was used. The arrangement of the laser photoablation system has been previously described [14]. The pulse-to-pulse amplitude fluctuation was 15% as measured by an oscilloscope. A beam analysis system with a pyroelectric detector array (CQ3D, Spiricon, Logan, UT) was used to measure the beam profile. After passing through three harmonic generating crystals, the beam intensity distribution was highly irregular with several spikes (hot spots) (Fig. 1a). A calcium fluoride (CaF_2) lens with a focal length of 2 meters was added at the output of the laser to focus the ultraviolet beam. Although the near field intensity was irregular, the beam still could be considered a "plane-wave." At the focus plane, the intensity distribution was a near diffraction-limited focal spot [16] of $\sim 0.5 \text{ mm}$ in diameter. The Spiricon beam detector and computer simulation revealed a smooth quasi-Gaussian beam distribution with a correlation coefficient of 0.95 (Fig. 1b). The crater created by this beam on PMMA had a

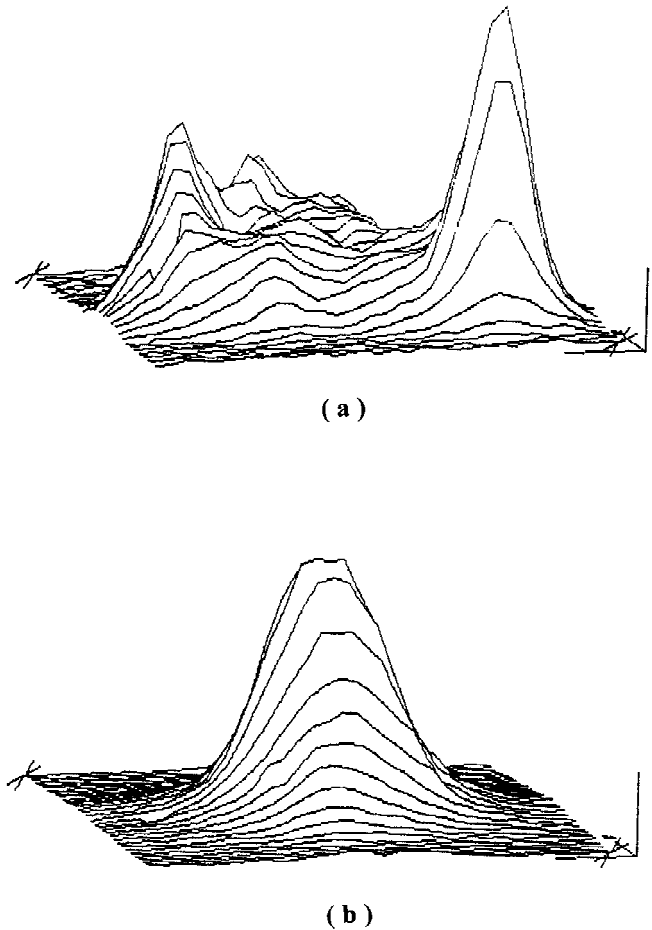


Fig. 1. Beam profile of the frequency-quintupled Nd:YAG laser (213 nm) measured with a beam analysis system using a pyroelectric array detector (CQ-3D, Spiricon, Inc., Logan, UT): (a) The beam profile measured without the 2 m lens. The beam was irregular with several spikes (hot spots). (b) The lens transformed the UV beam to a quasi-Gaussian profile with a correlation coefficient of 0.95.

smooth profile as measured by a three-dimensional scanning probe microscope (WYKO Corp., Tucson, AZ) (Fig. 2).

To determine the peak radiant exposure of the fifth harmonic (213 nm) beam, a metal pinhole with $100 \mu\text{m}$ diameter was placed at the center of the beam. The average energy of 100 pulses that passed through the pinhole was measured with a calibrated energy meter (JD-500, Molecron, Portland, OR). The radiant exposure at the beam center was calculated by dividing the energy by the area of the pinhole. If we assume that the beam has a Gaussian distribution, then the radiant exposure can be expressed as:

$$F(x,y) = F_0 \exp\{-2(x^2 + y^2)/r^2\}$$

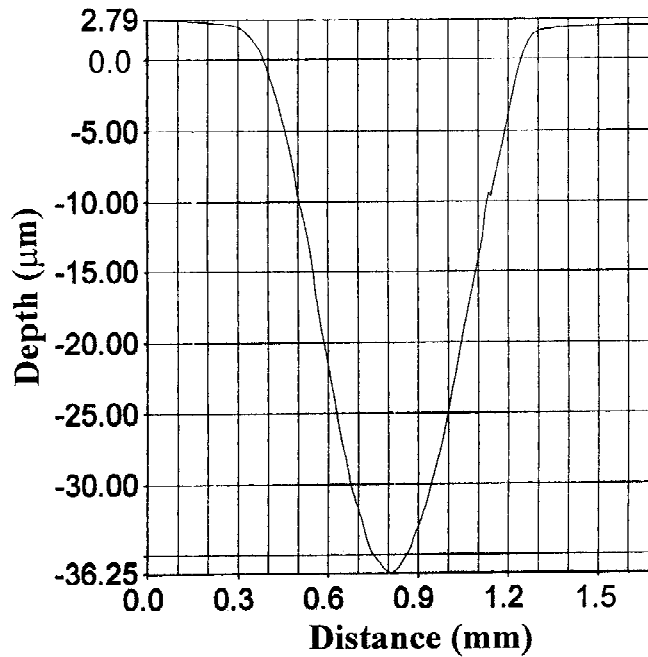


Fig. 2. Typical example of the cross section through the diameter of the crater produced by a series of pulses of the quasi-Gaussian 213 nm beam on PMMA. (The measurement was performed by WYKO Corp., Tucson, AZ).

where x and y is the spatial coordinate, F_0 is the beam central radiant exposure, and r is the $1/e^2$ beam radius. Since the measured energy that passed through the pinhole was 1.5–3% of the entire pulse energy, calculation showed that the averaged radiant exposure inside the pinhole was over 97% of the peak radiant exposure F_0 [17].

Sample Preparation

PMMA. These films with thickness of $260 \pm 5 \mu\text{m}$ were prepared by precision milling. The thickness was measured by a micrometer.

Cornea. Ten fresh human cadaver eyes were used within 24 hours postmortem. The epithelium was carefully removed with a blunt knife. Before preparation, the thickness of the cornea was measured with an ultrasound pachymeter (Pachette, DGH Technologies, Frazer, PA) as an indication of the initial hydration condition ($< 600 \mu\text{m}$). From each cornea, two corneal lenticules $\sim 200 \mu\text{m}$ thick and 7 mm in diameter were sliced with a microkeratome (BKS-1000, Polytech GmbH, Darmstadt, Germany). The first layer contained Bowman's layer and superficial stroma, and the second layer contained only mid-stroma. The thickness of the corneal lenticules was measured with the mechanical pachymeter (accuracy $\pm 10 \mu\text{m}$, Mitotuyo, Japan) provided

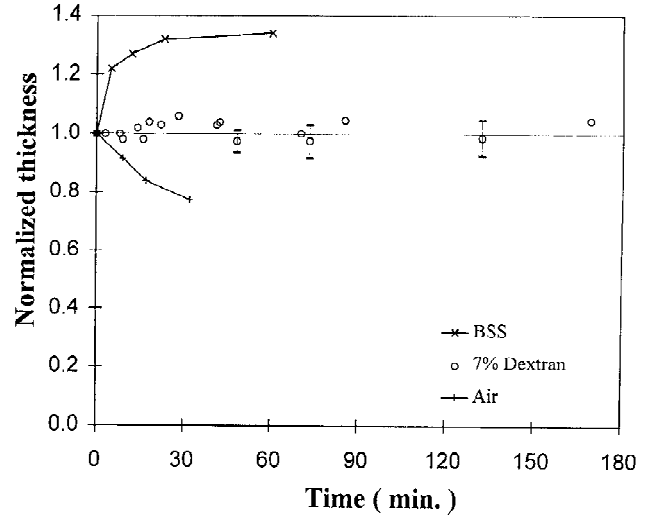


Fig. 3. Stability of the corneal lenticule thickness for lenticules stored in air, with the lens paper moistened by balanced salt solution (BSS), and 7% Dextran solution.

with the BKS-1000 instrument set. All samples were between $160 \mu\text{m}$ and $210 \mu\text{m}$ thick. During this procedure, 7% Dextran was used as a lubricant for the microkeratome. After the corneal samples were cut, they were placed on clean lens paper moistened with 7% Dextran and covered in a petri dish. A preliminary study showed that with this storage method, the thickness of the corneal tissue could be maintained constant for > 3 hours (Fig. 3).

Ablation Experiment

The experimental setup for the ablation experiment is shown in Figure 4. For a given radiant exposure, the ablation rates were calculated by dividing the thickness of the samples by the number of pulses needed for perforation. The perforation occurred at the time of the emission of blue fluorescent light from an underlying white paper. A computer-controlled shutter was manually triggered to stop the laser irradiation and display the number of pulses when the blue light was observed. The operator's reaction time was normally ~ 0.5 second, which lead to a variation of 2–5 pulses. The radiant exposure was varied by inserting different pieces of quartz and calcium fluoride (CaF_2) glass slides in the beam path.

Two PMMA samples were ablated. For each sample, the ablation rate was measured at 11 different radiant exposure levels covering the entire available radiant exposure range (72–507 mJ/

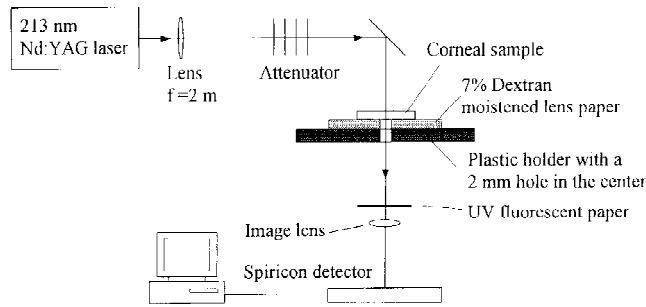


Fig. 4. Experimental setup for corneal ablation rate measurement. The image lens and the Spiricon detector were only used when measuring beam intensity profile.

cm²). Two measurements were made for each radiant exposure level.

Sixteen corneal samples were smoothly cut from ten human cadaver eyes. For each sample, the ablation rate was measured at seven different radiant exposure levels covering most of the available radiant exposure range (72–507 mJ/cm²). At each radiant exposure level, at least five samples were tested, and two measurements were made and averaged for each sample. The corneal samples were always kept in the covered petri dishes as described previously, except during the ablation procedure. After each perforation, the thickness of the sample was measured with the BKS mechanical pachymeter. Because the sample thickness may decrease during a long irradiation exposure, the average thickness before and after ablation was used for the calculation.

RESULTS

PMMA. The ablation rate of PMMA at 213 nm is shown in Figure 5. The ablation threshold of PMMA was below our lowest measured radiant exposure of 72 mJ/cm². The ablation rate was 0.10 ± 0.01 $\mu\text{m/pulse}$ at 100 mJ/cm², 0.31 ± 0.01 $\mu\text{m/pulse}$ at 203 mJ/cm², and it increased almost linearly to 0.40 ± 0.01 $\mu\text{m/pulse}$ at 256 mJ/cm². The ablation rate reached 0.50 ± 0.01 $\mu\text{m/pulse}$ at 345 mJ/cm². At our highest radiant exposure level of 507 mJ/cm², the ablation rate was 0.62 ± 0.01 $\mu\text{m/pulse}$.

Cornea. The corneal tissue ablation rate at 213 nm is shown in Figure 6. The mean and the standard deviation (mean \pm SD) were analyzed for each measured radiant exposure. No significant difference was found between the superficial corneal and midstromal groups. The data

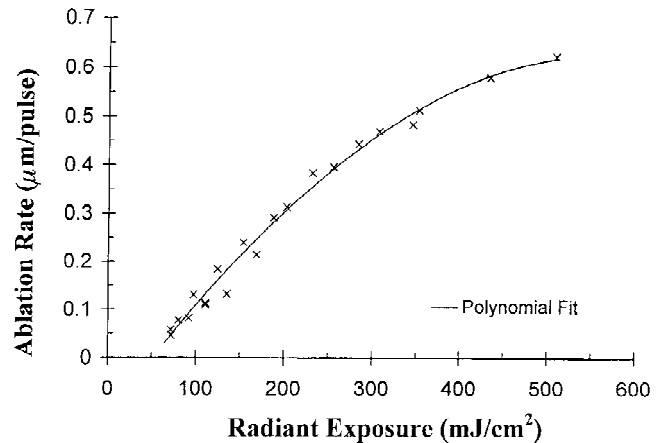


Fig. 5. Ablation rate of PMMA as a function of radiant exposure with the frequency-quintupled Nd:YAG laser (213 nm). The solid line is the computer-generated, best-fit polynomial curve of all points.

showed that the ablation threshold for cornea was below the lowest tested radiant exposure of 72 mJ/cm². Cornea had an ablation rate of 0.11 ± 0.04 $\mu\text{m/pulse}$ at 98 mJ/cm², 0.34 ± 0.18 $\mu\text{m/pulse}$ at 188 mJ/cm², 0.96 ± 0.14 $\mu\text{m/pulse}$ at 304 mJ/cm², 1.18 ± 0.20 $\mu\text{m/pulse}$ at 353 mJ/cm², and 1.49 ± 0.16 $\mu\text{m/pulse}$ at 507 mJ/cm².

DISCUSSION

Different lasers have been used to study the ablation rate of cornea tissue [5–9,18–25]. Two methods were most commonly used. Either the pulses required to perforate corneas of known thickness were counted, or the depths of ablation with fixed numbers of pulses were measured. There were problems with each of these methods. For both methods, the corneal thickness or the depths of ablation were influenced by variations in the hydration states of the corneal tissues during the experiments [26]. Most studies did not indicate if corneal hydration was controlled. Additionally, the beam intensity distributions in many studies were not completely uniform, even if the most uniform parts of the laser beams were selected by masking. Therefore, there were hot spots within the beams, so that the radiant exposure could only be determined approximately [25]. These hot spots posed an additional problem for the first ablation method, since the exact number of pulses required for perforation only could be estimated. Tissue shrinkage artifacts also may occur during the second method of ablation determination. Changing the focus of a microscope to

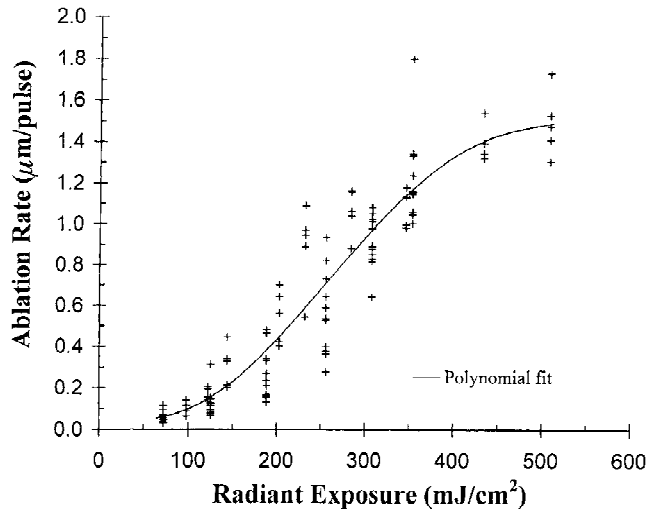


Fig. 6. Ablation rate of human cornea as a function of radiant exposure with the frequency-quintupled Nd:YAG laser (213 nm). The solid line is the computer-generated best-fit polynomial curve of all points.

gauge the ablation depth [25] or measurements on fixed tissue sections may be inaccurate following processing for histology.

By converting the irregular laser beam into a 95% Gaussian beam and using the central peak of the beam to determine the radiant exposure, we minimized the possible error induced by the beam inhomogeneity in the ablation rate study. Gaussian beam profile offers an advantage for corneal reshaping using a scanning delivery system. The energy profile for the removal of known corneal tissue can be mathematically expressed by the Gaussian series. With a known ablation rate, the ablation algorithm can be theoretically derived and applied to the scanning beam delivery system [27].

The ablation of PMMA at 213 nm showed a similar behavior to that at 193 nm [28], and was different from that at 248 nm (Fig. 7). We estimate that the PMMA ablation threshold with 213 nm was ~ 50 mJ/cm², which is the same as that at 193 nm [28]. The ablation rates at both wavelengths increased nearly linearly with radiant exposure up to ~ 250 mJ/cm². At this point, the ablation rate was 0.4 μ m/pulse at 213 nm, and 0.25 to 0.4 μ m/pulse at 193 nm. At 400 mJ/cm², the ablation rate reached ~ 0.55 μ m/pulse at 213 nm, and ~ 0.3 – 0.4 μ m/pulse at 193 nm. Measurements of PMMA ablation rates at 213 nm by other groups with different methods [29,30] showed similar results (Fig. 7).

The variation of cornea ablation in our study

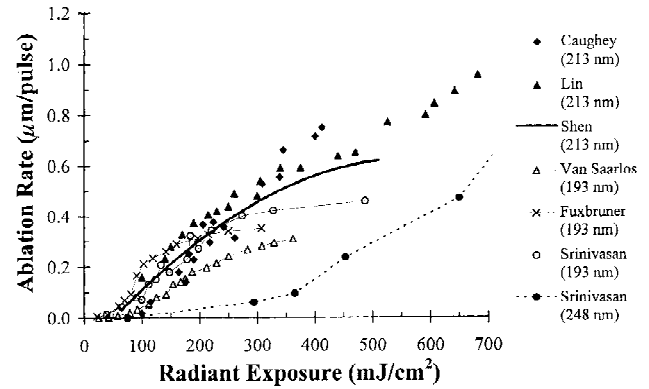


Fig. 7. Comparison of PMMA ablation rates at 213 nm, 193 nm, and 248 nm by different investigators.

might be caused by surface irregularity and unevenness of the mechanically cut corneal lenticles, resulting in thickness variations in the same cornea sample. Although hydration was carefully controlled, corneal hydration changes during the experiment could have contributed to the variability of the ablation rate study. Another possible source of error was mechanical tearing due to the lateral stresses on the ablation site when the sample was almost perforated. This phenomenon could cause an overestimation of the ablation rate.

The characteristics of corneal ablation using the frequency-quintupled Nd:YAG laser (213 nm) and the ArF excimer lasers (193 nm) were similar (Fig. 8). At 193 nm, the corneal ablation threshold measured by different research groups varied from 30 mJ/cm² [25] to 50 mJ/cm² [5,18]. We found that the cornea ablation threshold for the 213 nm was < 72 mJ/cm² and the ablation rate curve appearance (Fig. 8) suggests that it might be < 50 mJ/cm². When the radiant exposure was below 200 mJ/cm², the ablation rates of 213 nm and 193 nm were similar [5,21–23,25]. For example, at 120 mJ/cm², the ablation rates of 213 nm and 193 nm were both in the range of 0.12–0.17 μ m per pulse. However, the ablation rate of 213 nm increased gradually faster as radiant exposure increased when compared with the 193 nm excimer laser [5,18,19,21–25]. When the radiant exposure was increased over 250 mJ/cm², the ablation rate for 213 nm was between 1.2 and 2.2 times faster than the ablation rate for 193 nm (Fig. 8).

In photo-refractive keratectomy (PRK), precise removal of corneal tissue and minimal change of ablation rate with fluctuations of radi-

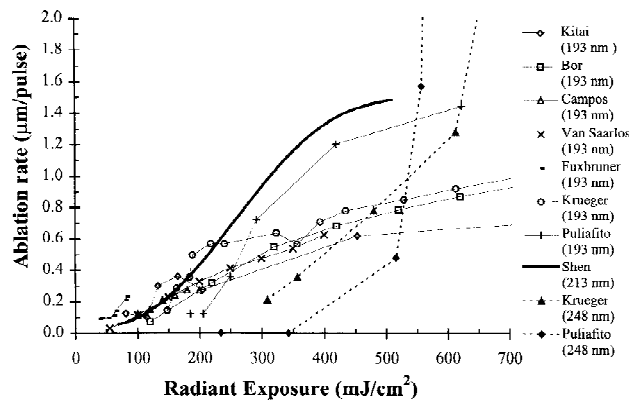


Fig. 8. Comparison of corneal ablation rates at 213 nm, 193 nm, and 248 nm by different investigators.

ant exposure are required. Therefore, low level radiant exposure with a small ablation rate slope is preferred. For example, current commercial PRK procedures using 193 nm excimer laser normally select radiant exposure between 160 and 180 mJ/cm², which correspond to ~ 0.22–0.25 μm per pulse ablation rates [31]. The radiant exposure level of 213 nm should be selected between 125 mJ/cm² and 175 mJ/cm² to produce the ablation rate between 0.15 and 0.30 μm per pulse.

PMMA and corneal ablation characteristics at 248 nm within the measured radiant exposure range (<507 mJ/cm²) were considerably different from ablation at 213 nm and 193 nm (Figs. 7, 8). The ablation rates for PMMA and cornea at 248 nm showed an exponential curve rather than a logarithmic curve [5,19]. The collateral damage created by 248 nm is also much deeper than that created by 213 nm and 193 nm [19].

Our study also showed that the ablation characteristics of PMMA differ from that of cornea at 213 nm. This may be explained by the structural difference between PMMA and cornea. PMMA material is pure cross-linked methyl methacrylate organic molecules. The main ablation steps are light absorption, molecular bond breaking, and debris removal. The ablation rate tends to saturate with the increase of the radiant exposure because of the limitation of the energy penetration depth. Corneal tissues are composed of collagen fibrils with bound water. Water does not strongly absorb at 213 nm [32]. Ultraviolet laser pulses are absorbed by the collagen molecules and detach the molecules and macromolecules from their neighbors by breaking the molecular bond or mechanical stresses. To start the

ablation process, extra UV energy is needed to break the hindrance of water by either vaporizing the water or an explosive blast [33]. With increasing radiant exposure, the extra portion of UV energy increases, which results in the ablation rate curvature appearing exponential at the lower radiant exposure levels (<300 mJ/cm²). When the radiant exposure continuously increases, the limitation of energy penetration depth also saturates the ablation rate. The difference in graphed ablation rate curvatures between cornea and PMMA indicates that a beam with a Gaussian profile will create a smaller diameter hole in cornea than in PMMA when the radiant exposure is below 300 mJ/cm². If a scanning beam delivery system is used to ablate a smooth surface, then, a smaller pulse-to-pulse distance will be needed on cornea than on PMMA. When the radiant exposure is bigger than 150 mJ/cm², the cornea has a higher ablation rate than PMMA. This difference in ablation rates indicates that the cornea would be overcorrected if PMMA is used directly to calibrate the laser ablation algorithm for PRK.

The data presented here provides a measurement of the ablation rate of PMMA and human corneal tissue for the frequency-quintupled Nd:YAG laser (213 nm). However, there are still some parameters not yet considered. The effects of variation of corneal hydration on the tissue ablation rate and the difference in ablation rate between Bowman's layer and stroma are factors to consider for future in vivo studies. Nevertheless, our study provides useful guidance for clinical application.

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